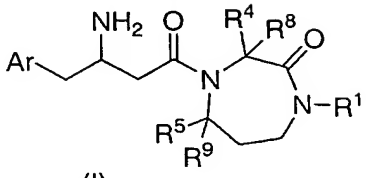
WHAT IS CLAIMED IS:

1. A compound of the formula I:



(I)

or a pharmaceutically acceptable salt thereof; wherein
each n is independently 0, 1, or 2;

Ar is phenyl substituted with one to five $R^3$ substituents;

$R^1$ is selected from the group consisting of
hydrogen,
$C_{1-10}$ alkyl, wherein alkyl is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, $C_{1-6}$ alkoxy, carboxy, $C_{1-6}$ alkyloxycarbonyl, and phenyl-$C_{1-3}$ alkoxy, wherein alkoxy is unsubstituted or substituted with one to five halogens,
$(CH_2)_n$-aryl, wherein aryl is unsubstituted or substituted with one to five substituents independently selected from halogen, CN, hydroxy, $R^2$, $OR^2$, $NHSO_2R^2$, $NR^2SO_2R^2$, $SO_2R^2$, $CO_2H$, and $C_{1-6}$ alkyloxycarbonyl,
$(CH_2)_n$-heteroaryl, wherein heteroaryl is unsubstituted or substituted with one to three substituents independently selected from hydroxy, halogen, $C_{1-6}$ alkyl, and $C_{1-6}$ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,
$(CH_2)_n$-heterocyclyl, wherein heterocyclyl is unsubstituted or substituted with one to three substituents independently selected from oxo, hydroxy, halogen, $C_{1-6}$ alkyl, and $C_{1-6}$ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,
$(CH_2)_n$-$C_{3-6}$ cycloalkyl, wherein cycloalkyl is unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy, $C_{1-6}$ alkyl, and $C_{1-6}$ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens; and

wherein any methylene ($CH_2$) carbon atom in $R^1$ is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and $C_{1-4}$ alkyl unsubstituted or substituted with one to five halogens;

each $R^3$ is independently selected from the group consisting of
hydrogen,
halogen,
cyano,
hydroxy,
$C_{1-6}$ alkyl, unsubstituted or substituted with one to five halogens,
$C_{1-6}$ alkoxy, unsubstituted or substituted with one to five halogens,
carboxy,
alkoxycarbonyl,
amino,
$NHR^2$,
$NR^2R^2$,
$NHSO_2R^2$,
$NR^2SO_2R^2$,
$NHCOR^2$,
$NR^2COR^2$,
$NHCO_2R^2$,
$NR^2CO_2R^2$,
$SO_2R^2$,
$SO_2NH_2$,
$SO_2NHR^2$, and
$SO_2NR^2R^2$;

each $R^2$ is independently $C_{1-6}$ alkyl, unsubstituted or substituted with one to five substituents independently selected from halogen, $CO_2H$, and $C_{1-6}$ alkyloxycarbonyl;

$R^4$ and $R^5$ are independently selected from the group consisting of:
hydrogen,
cyano,
carboxy,

$C_{1-6}$ alkyloxycarbonyl,

$C_{1-10}$ alkyl, unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, $C_{1-6}$ alkoxy, carboxy, $C_{1-6}$ alkyloxycarbonyl, and phenyl-$C_{1-3}$ alkoxy, wherein alkoxy is unsubstituted or substituted with one to five halogens,

$(CH_2)_n$-aryl, wherein aryl is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, $C_{1-6}$ alkyl, and $C_{1-6}$ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

$(CH_2)_n$-heteroaryl, wherein heteroaryl is unsubstituted or substituted with one to three substituents independently selected from hydroxy, halogen, $C_{1-6}$ alkyl, and $C_{1-6}$ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

$(CH_2)_n$-heterocyclyl, wherein heterocyclyl is unsubstituted or substituted with one to three substituents independently selected from oxo, hydroxy, halogen, $C_{1-6}$ alkyl, and $C_{1-6}$ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

$(CH_2)_n$-$C_{3-6}$ cycloalkyl, wherein cycloalkyl is unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy, $C_{1-6}$ alkyl, and $C_{1-6}$ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

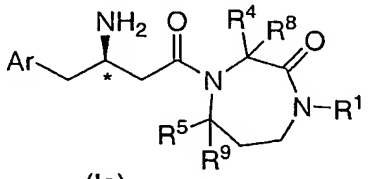
$(CH_2)_nCONR^6R^7$, wherein $R^6$ and $R^7$ are independently selected from the group consisting of hydrogen, tetrazolyl, thiazolyl, $(CH_2)_n$-phenyl, $(CH_2)_n$-$C_{3-6}$ cycloalkyl, and $C_{1-6}$ alkyl, wherein alkyl is unsubstituted or substituted with one to five halogens and wherein phenyl and cycloalkyl are unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, $C_{1-6}$ alkyl, and $C_{1-6}$ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens;

or wherein $R^6$ and $R^7$ together with the nitrogen atom to which they are attached form a heterocyclic ring selected from azetidine, pyrrolidine, piperidine, piperazine, and morpholine; and wherein said heterocyclic ring is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, $C_{1-6}$ alkyl, and $C_{1-6}$ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens; and wherein any methylene ($CH_2$) carbon atom in $R^4$ or $R^5$ is unsubstituted or

substituted with one to two groups independently selected from halogen, hydroxy, and $C_{1-4}$ alkyl unsubstituted or substituted with one to five halogens; and

$R^8$ and $R^9$ are each independently hydrogen or $C_{1-6}$ alkyl.

2. The compound of Claim 1 of the formula Ia:




(Ia)

wherein the carbon atom marked with an * has the *R* configuration and Ar, $R^1$, $R^4$, $R^5$, $R^8$, and $R^9$ are as defined in Claim 1.

3. The compound of Claim 1 wherein $R^3$ is selected from the group consisting of

hydrogen,
halogen,
cyano,
hydroxy,
$C_{1-6}$ alkyl, unsubstituted or substituted with one to five halogens, and
$C_{1-6}$ alkoxy, unsubstituted or substituted with one to five halogens.

4. The compound of Claim 3 wherein $R^3$ is selected from the group consisting of hydrogen, fluoro, chloro, bromo, trifluoromethyl, and methyl.

5. The compound of Claim 4 wherein $R^3$ is hydrogen, chloro, or fluoro.

6. The compound of Claim 1 wherein $R^1$ is selected from the group consisting of:

hydrogen,
$C_{1-6}$ alkyl, wherein alkyl is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, $C_{1-6}$ alkoxy, carboxy, $C_{1-6}$

alkyloxycarbonyl, and phenyl-$C_{1-3}$ alkoxy, wherein alkoxy is unsubstituted or substituted with one to five halogens,

$(CH_2)_n$-$C_{3-6}$ cycloalkyl, wherein cycloalkyl is unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy, $C_{1-6}$ alkyl, and $C_{1-6}$ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens; and

wherein any methylene ($CH_2$) carbon atom in $R^1$ is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and $C_{1-4}$ alkyl unsubstituted or substituted with one to five halogens.

7. The compound of Claim 6 wherein $R^1$ is selected from the group consisting of

hydrogen,
$C_{1-4}$ alkyl,
2,2,2-trifluoroethyl,
methoxycarbonylmethyl,
carboxymethyl,
hydroxyethyl,
benzyloxymethyl,
benzyloxyethyl, and
cyclopropyl.

8. The compound of Claim 7 wherein $R^1$ is selected from the group consisting of hydrogen, methyl, *tert*-butyl, and cyclopropyl.

9. The compound of Claim 1 wherein $R^4$ and $R^5$ are independently selected from the group consisting of:

hydrogen,
$C_{1-10}$ alkyl, unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, $C_{1-6}$ alkoxy, carboxy, $C_{1-6}$ alkyloxycarbonyl, and phenyl-$C_{1-3}$ alkoxy, wherein alkoxy is unsubstituted or substituted with one to five halogens,
$(CH_2)_n$-aryl, wherein aryl is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, $C_{1-6}$ alkyl, and $C_{1-6}$ alkoxy,

wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

$(CH_2)_n$-heteroaryl, wherein heteroaryl is unsubstituted or substituted with one to three substituents independently selected from hydroxy, halogen, $C_{1-6}$ alkyl, and $C_{1-6}$ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

$(CH_2)_n$-heterocyclyl, wherein heterocyclyl is unsubstituted or substituted with one to three substituents independently selected from oxo, hydroxy, halogen, $C_{1-6}$ alkyl, and $C_{1-6}$ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

$(CH_2)_n$-$C_{3-6}$ cycloalkyl, wherein cycloalkyl is unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy, $C_{1-6}$ alkyl, and $C_{1-6}$ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

wherein any methylene ($CH_2$) carbon atom in $R^4$ or $R^5$ is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and $C_{1-4}$ alkyl unsubstituted or substituted with one to five halogens.

10. The compound of Claim 9 wherein $R^4$ and $R^5$ are independently selected from the group consisting of:

hydrogen,

$C_{1-6}$ alkyl, unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, $C_{1-6}$ alkoxy, carboxy, $C_{1-6}$ alkyloxycarbonyl, and phenyl-$C_{1-3}$ alkoxy, wherein alkoxy is unsubstituted or substituted with one to five halogens,

$(CH_2)_n$-aryl, wherein aryl is unsubstituted or substituted with one to five substituents independently selected from halogen, hydroxy, $C_{1-6}$ alkyl, and $C_{1-6}$ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

$(CH_2)_n$-heteroaryl, wherein heteroaryl is unsubstituted or substituted with one to three substituents independently selected from hydroxy, halogen, $C_{1-6}$ alkyl, and $C_{1-6}$ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens,

$(CH_2)_n$-$C_{3-6}$ cycloalkyl, wherein cycloalkyl is unsubstituted or substituted with one to three substituents independently selected from halogen, hydroxy, $C_{1-6}$ alkyl, and

$C_{1-6}$ alkoxy, wherein alkyl and alkoxy are unsubstituted or substituted with one to five halogens, and

wherein any methylene ($CH_2$) carbon atom in $R^4$ or $R^5$ is unsubstituted or substituted with one to two groups independently selected from halogen, hydroxy, and $C_{1-4}$ alkyl unsubstituted or substituted with one to five halogens.

11. The compound of Claim 10 wherein $R^4$ and $R^5$ are independently selected from the group consisting of:

hydrogen,
$CH_3$,
$CH_2CH_3$,
$CH_2CH(CH_3)_2$,
$CH_2$-cyclopropyl,
$CH_2$-cyclohexyl,
$CH_2OCH_2Ph$,
$CH_2OH$
$CH_2Ph$,
$CH_2$(3-$OCF_3$-Ph),
$CH_2$(4-$OCF_3$-Ph),
$CH_2$(3-$CF_3$,5-$CF_3$-Ph),
$CH_2$(2-$CF_3$-Ph),
$CH_2$(2-Cl-Ph),
$CH_2$(2-Me-Ph),
$CH_2$(2-Me,5-Me-Ph),
$CH_2$(2-Ph-Ph),
$CH_2$(2-F,5-F-Ph),
$CH_2$(2-F-Ph),
$CH_2$(2-F,3-F-Ph),
$CH_2$(2-pyridinyl),
$CH_2$(3-pyridinyl),
$CH_2$(4-pyridinyl),
$CH_2$(1-oxidopyridin-2-yl),
$CH_2$(1-oxidopyridin-3-yl),
$CH_2$(1*H*-pyrazol-1-yl),
$CH_2$(2-F,6-F-Ph), and

$CH_2CF_3$.

12. The compound of Claim 11 wherein $R^5$ is hydrogen.

13. The compound of Claim 1 wherein $R^8$ and $R^9$ are independently selected from hydrogen and methyl.

14. The compound of Claim 13 wherein $R^8$ and $R^9$ are hydrogen.

15. The compound of Claim 1 wherein $R^1$ is selected from the group consisting of

hydrogen,
$C_{1-4}$ alkyl,
2,2,2-trifluoroethyl,
methoxycarbonylmethyl,
carboxymethyl,
hydroxyethyl,
benzyloxymethyl,
benzyloxyethyl, and
cyclopropyl;

$R^3$ is hydrogen, chloro, or fluoro;

$R^4$ is selected from the group consisting of:

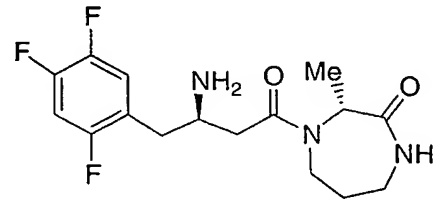
hydrogen,
$CH_3$,
$CH_2CH_3$,
$CH_2CH(CH_3)_2$,
$CH_2$-cyclopropyl,
$CH_2$-cyclohexyl,
$CH_2OCH_2Ph$,
$CH_2OH$
$CH_2Ph$,
$CH_2$(3-$OCF_3$-Ph),
$CH_2$(4-$OCF_3$-Ph), and
$CH_2$(3-$CF_3$,5-$CF_3$-Ph)
$CH_2$(2-$CF_3$-Ph),

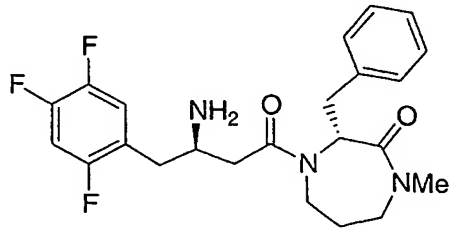
$CH_2$(2-Cl-Ph),
$CH_2$(2-Me-Ph),
$CH_2$(2-Me,5-Me-Ph),
$CH_2$(2-Ph-Ph),
$CH_2$(2-F,5-F-Ph),
$CH_2$(2-F-Ph),
$CH_2$(2-F,3-F-Ph),
$CH_2$(2-pyridinyl),
$CH_2$(3-pyridinyl),
$CH_2$(4-pyridinyl),
$CH_2$(1-oxidopyridin-2-yl),
$CH_2$(1-oxidopyridin-3-yl),
$CH_2$(1*H*-pyrazol-1-yl),
$CH_2$(2-F,6-F-Ph), and
$CH_2CF_3$; and

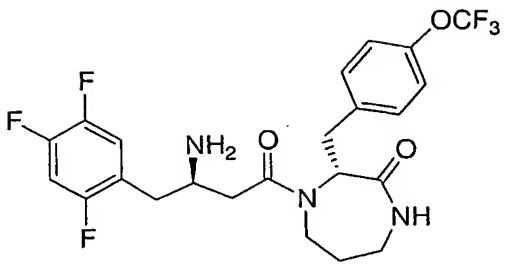
$R^8$ and $R^9$ are hydrogen.

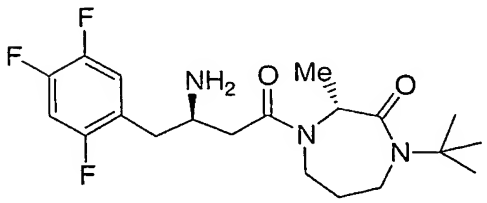
16. The compound of Claim 15 wherein $R^5$ is hydrogen.

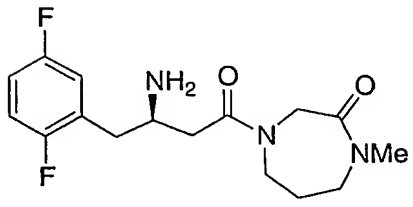
17. The compound of Claim 15 which is selected from the group consisting of



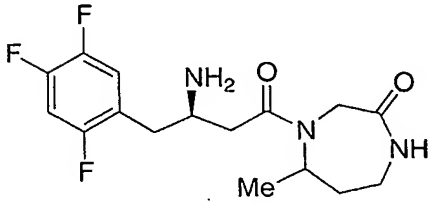







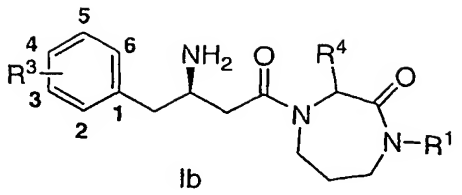


and



or a pharmaceutically acceptable salt thereof.

18. The compound of Claim 15 of structural formula Ib selected from the group consisting of



Ib

| $R^3$ | $R^4$ | $R^1$ |
|---|---|---|
| 2-F, 5-F | Me | H |
| 2-F, 4-F, 5-F | $CH_2$-*c*Pr | H |
| 2-F, 4-F, 5-F | Me | Me |
| 2-F, 5-F | Me | Et |
| 2-F, 4-F, 5-F | Me | *c*Pr |
| 2-F, 5-F | Me | $CH_2CO_2Me$ |
| 2-F, 4-F, 5-F | Me | $CH_2CH_2OH$ |
| 2-F, 4-F, 5-F | Me | $CH_2CH_2OCH_2C_6H_5$ |
| 2-F, 4-F, 5-F | Et | Me |
| 2-F, 5-F | Et | Me |
| 2-F, 4-F, 5-F | $CH_2OH$ | Me |
| 2-F | $CH_2Ph$ | Me |
| 3-F, 4-F | $CH_2Ph$ | Me |
| 2-F, 4-F, 5-F | $CH_2OCH_2Ph$ | Me |
| 2-F, 4-F, 5-F | Et | H |
| 2-F, 4-F, 5-F | $CH_2Ph$ | H |
| 3-F, 4-F | $CH_2Ph$ | H |
| 2-F, 5-F | $CH_2$(4-$OCF_3$-Ph) | H |
| 2-F, 4-F, 5-F | $CH_2$(3-$OCF_3$-Ph) | H |
| 2-F, 4-F, 5-F | $CH_2CH(CH_3)_2$ | Me |

| | | |
|---|---|---|
| 2-F, 4-F, 5-F | $CH_2$(3-$CF_3$,5-$CF_3$-Ph) | H |
| 2-F, 5-F | H | H |
| 2-F, 4-F, 5-F | $CH_2$(2-$CF_3$-Ph) | H |
| 2-F, 4-F, 5-F | $CH_2$(2-Cl-Ph) | H |
| 2-F, 4-F, 5-F | $CH_2$(2-$CH_3$-Ph) | H |
| 2-F, 4-F, 5-F | $CH_2$(2-$CH_3$,5-$CH_3$-Ph) | H |
| 2-F, 4-F, 5-F | Me | $CHMe_2$ |
| 2-F, 4-F, 5-F | $CH_2$(2-Ph-Ph) | H |
| 2-F, 4-F, 5-F | $CH_2$(2-F,5-F-Ph) | H |
| 2-F, 4-F, 5-F | $CH_2$(2-F-Ph) | H |
| 2-F, 4-F, 5-F | Me | $CH_2CF_3$ |
| 2-F, 4-F, 5-F | $CH_2$(2-F,3-F-Ph) | H |
| 2-F, 4-F, 5-F | $CH_2$(3-pyridyl) | H |
| 2-F, 4-F, 5-F | $CH_2$(2-F-Ph) | $CH_2CH_2CH_3$ |
| 2-F, 4-F, 5-F | $CH_2$(4-pyridyl) | H |
| 2-F, 4-F, 5-F | $CH_2$(2-F-Ph) | Me |
| 2-F, 4-F, 5-F | $CH_2$(2-pyridyl) | H |
| 2-F, 4-F, 5-F | $CH_2$(2-F,6-F-Ph) | H |
| 2-F, 4-F, 5-F | $CH_2CF_3$ | H |

or a pharmaceutically acceptable salt thereof.

19. A pharmaceutical composition which comprises a compound of Claim 1 and a pharmaceutically acceptable carrier.

20. A method for inhibiting dipeptidyl peptidase-IV enzyme activity in a mammal in need thereof which comprises the administration to the mammal of an effective amount of a compound of Claim 1.

21. A method for treating diabetes in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

22. A method for treating non-insulin dependent (Type 2) diabetes in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

23. A method for treating hyperglycemia in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

24. A method for treating obesity in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

25. A method for treating one or more lipid disorders selected from the group of dyslipidemia, hyperlipidemia, hypertriglyceridemia, hypercholesterolemia, low HDL and high LDL in a mammal in need thereof which comprises the administration to the mammal of a therapeutically effective amount of a compound of Claim 1.

26. A method for treating in a mammal in need thereof one or more conditions selected from the group consisting of (1) hyperglycemia, (2) low glucose tolerance, (3) insulin resistance, (4) obesity, (5) lipid disorders, (6) dyslipidemia, (7) hyperlipidemia, (8) hypertriglyceridemia, (9) hypercholesterolemia, (10) low HDL levels, (11) high LDL levels, (12) atherosclerosis and its sequelae, (13) vascular restenosis, (14) irritable bowel syndrome, (15) inflammatory bowel disease, including Crohn's disease and ulcerative colitis, (16) other inflammatory conditions, (17) pancreatitis, (18) abdominal obesity, (19) neurodegenerative disease, (20) retinopathy, (21) nephropathy, (22) neuropathy, (23) Syndrome X, (24) ovarian hyperandrogenism (polycystic ovarian syndrome), and other disorders where insulin resistance is

a component, wherein the method comprises the administration to the mammal a therapeutically effective amount of a compound of Claim 1.

27. The pharmaceutical composition of Claim 19 further comprising one or more additional active ingredients selected from the group consisting of:

(a) a second dipeptidyl peptidase IV inhibitor;

(b) an insulin sensitizer selected from the group consisting of a PPARγ agonist, a PPARα/γ dual agonist, a PPARα agonist, a biguanide, and a protein tyrosine phosphatase-1B inhibitor;

(c) an insulin or insulin mimetic;

(d) a sulfonylurea or other insulin secretagogue;

(e) an α-glucosidase inhibitor;

(f) a glucagon receptor antagonist;

(g) GLP-1, a GLP-1 mimetic, or a GLP-1 receptor agonist;

(h) GIP, a GIP mimetic, or a GIP receptor agonist;

(i) PACAP, a PACAP mimetic, or a PACAP receptor agonist;

(j) a cholesterol lowering agent such as (i) HMG-CoA reductase inhibitor, (ii) sequestrant, (iii) nicotinyl alcohol, nicotinic acid or a salt thereof, (iv) PPARα agonist, (v) PPARα/γ dual agonist, (vi) inhibitor of cholesterol absorption, (vii) acyl CoA:cholesterol acyltransferase inhibitor, and (viii) anti-oxidant;

(k) a PPARδ agonist;

(l) an antiobesity compound;

(m) an ileal bile acid transporter inhibitor;

(n) an anti-inflammatory agent; and

(o) an antihypertensive agent.

28. The pharmaceutical composition of Claim 27 wherein the PPARα/γ dual agonist is KRP-297.

29. A method of treating diabetes in a mammal in need thereof comprising administering to the mammal a therapeutically effective amount of a compound of Claim 1 in combination with the PPARα/γ dual agonist KRP-297.